

November 18, 1949.

Dr. David M. Bonner,  
Research Associate [?]  
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New Haven, Connecticut.

Dear Dave:

I am very much interested that you have succeeded in demonstrating antilactase antibodies. Could you send me a word about your techniques? We did a few very sloppy experiments a year or so ago, but failed to find any specific inhibitions of K-12 lactase by sera from rabbits injected with intact K-12 grown on lactose.

I have just been finishing up my work on K-12 lactase. We found, true enough, that very considerable lactase (10-20% of adaptive) is produced by K-12 grown on plain peptone, or on carbon sources other than glucose, including maltose and succinate. Much less is produced on glucose, probably owing to Sol's "competition." What has been holding me up so long is the fact that assays on dried or benzene-treated cells run about thirty times as high as on the same aliquots of intact cells, regardless of the type of cell they are (Lac+ unadapted or adapted, Lac<sub>1</sub>- adapted, etc.)

It should not be surprising that Y-53 (Lac<sub>1</sub>-) evokes antilactase sera, inasmuch as it produces substantial amounts (ca 5%) of lactase when grown on peptone-lactose media. As I mentioned last year, this strain produces ca 30-40% activity when grown on butyl and other galactosides. Before publishing any quantitative results, however, I want to be sure that I don't run into trouble on account of the "activation" by benzene, thymol, caprylic alcohol, drying, etc., and even by moderately concentrated buffer (M/10) or salts.

A number of genetically distinct Lac- mutations have been picked up here, as you know. I will be very glad to make them available to you for the experiments that you mentioned, provided that we can work out an arrangement that will forestall our breathing down each other's necks later on. We went after these strains for very much the same reasons, probably, that you have in mind, and if your temperament is at all like mine, Dave, you are going to be tempted to duplicate or anticipate my projected experiments, particularly if, as is likely true, you think that you can do some aspects of them better or quicker than I can. Would it be unreasonable

for me to ask you for a definite commitment that you will restrict your work on any strains that I send you to the specific purposes that you mentioned? You would certainly make me very uncomfortable if you induced the feeling, justifiable or not, that I had to be under some pressure with this work because OBL would otherwise take it over. On the other hand, my proprietary rights in this area are scarcely less limited than anyone else's, and I want to make it clear that I am asking these concessions of you much more as a personal favor than as a matter of very poorly defined "rights".

The areas of work that we are developing with the mutants and the onpg method are about as follows:

1. Kinetics, specificity and purification of lactase from Lac+.
2. Functional comparison of lactase in extracts and in intact cells.
3. Kinetics and specificity of adaptation mechanism vs. enzyme in Lac+, in partially blocked mutants, and in mutants with altered specificity
4. Genetic interactions in suppressor stocks
5. Specific and non-specific inhibition of adaptation.

If you are going to disperse your Neurospora program in favor of this direction of work in K-12, I think that it would be very appropriate for us to discuss the details first to avoid any unpleasantness later.

Under separate cover, I am sending W-45, which is a Lac<sub>2</sub>- mutant from 58-161. This should be especially suitable, inasmuch as it appears to be a completely "negative" mutant, and I have not been able to detect the slightest adaptation to lactose under any conditions.

You will undoubtedly be going to the AAAS meetings. We will be at the Gov. Clinton Hotel, in the event that we don't get together spontaneously. I hope that we will be able to discuss these matters in more detail over a few cases of beer.

With best regards,

Sincerely,

Joshua Lederberg